Systemic effects of acute inflammation

"Acute phase reaction"

Cytokines

TNF-α, IL-1, and IL-6

The most important mediators of acute phase reaction

Enumerate Systemic effects of acute inflammation

1. Fever
2. Leucocytosis
3. Elevated plasma of acute-phase proteins
4. Lymphangitis and Lymphadenitis
5. Shock
6. Other manifestations

1-Fever (*Explain mechanism of Fever)*

↑ body temperature (by 1° to 4°C),esp. with infection.

Mechanism

Bacterial products (exogenous pyrogens)

⇩

(+) leucocytes

⇩

release endogenous pyrogens (**IL-1 & TNF-α**)

⇩

↑production of **PGs**

In the hypothalamus, PGs

⇩

(+) production of neurotransmitters

⇩

reset the temp. set point at a higher level

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NSAIDs including aspirin ↓ fever by blocking PG synthesis.

2-Leucocytosis (Define)

bacterial infection

↑leucocyte count is usually up to 15,000 or 20,000 cells/ml

Mechanism:

- **TNF and IL1** accelerate the release of cells from BM reverse pool .
- **Activated macrophages & lymphocytes produce CSFs** →↑ BM

Production of leucocytes to compensate for those lost in the inflammatory reaction.

- ❑ **Most bacterial infections** → ***neutrophilia***
- ❑ **Viral infections**, as IMN, mumps &German measles → ***lymphocytosis***
- ❑ **Allergic reactions & parasitic infestations** → ***eosinophilia***
- ❑ Certain inf: Typhoid fever/viral **.>>> *Leucopenia***

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3-Elevated plasma levels of acute-phase proteins

- ❑ plasma proteins
- ❑ synthesized in the liver
- ❑ their conc. may ↑ up to 100-fold d.t inflammatory stimuli
- ❑ Synthesis by hepatocytes is mediated by **IL-6**.

- **C-reactive protein (CRP)**
- **Serum amyloid A (SAA) protien**

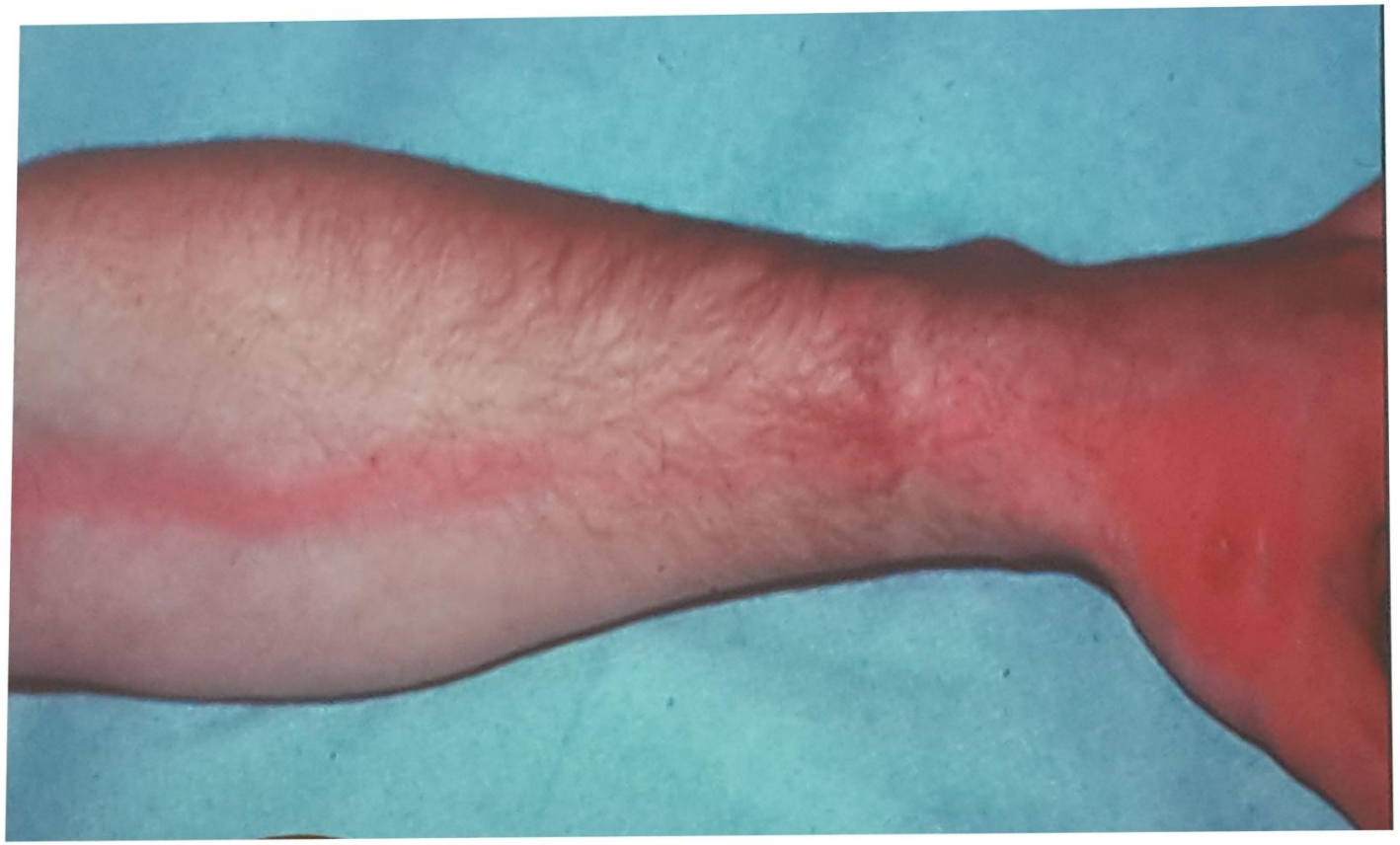
} **Opsonins**

Fibrinogen,>>> ESR elevated in inflammation

4-Lymphangitis and Lymphadenitis

Drain inflamed tissue

d.t mediators released from inflamed tissue or foreign antigen.



5-Shock

severe tissue injury or severe bacterial infections

↓

(+) production of enormous quantities of **TNF-α**

Profuse systemic V.D & ↑vascular permeability	Activation of coagulation pathway
↓	↓
hypotension & shock.	microthrombi throughout the body **("DIC")**

~~Other Manifestations~~

NSAIDs given to decrease pain block which of the following mediators

a) **Histamine**
b) **Prostaglandins**
c) **Serotonins**
d) **Nitric oxide species (NOS)**

Fate of acute inflammation

1. Resolution
2. Healing by fibrosis (scarring)
3. Progression
4. Chronic inflammation

2-Chronic inflammation

Definition

Inflammation of prolonged duration (weeks , months or years) in which → active inflammation

→ tissue injury

→ healing

occur at the same time

Cause :

1. **Progression from acute inflammation**
2. **Recurrent attacks of acute inflammation (cholecytitis)**

3- chronic inflammation from the start (starting de novo) :

1. Persistent infections by **micro-organisms that are difficult to eradicate**

2. **Autoimmune disease**

3. prolonged exposure to **potentially toxic agent eg silica**

.

Q) General features of chronic inflammation

- **Infiltration with**

macrophages , lymphocytes , plasma cells

- **Tissue destruction**

.

- **Endarteritis obliterans**

"EAO" : proliferation of intima narrowing of lumen

- **Proliferative changes ,**
- **angiogenesis**
- **Fibroblast proliferation**

>>> formation of granulation tissue & fibrosis

Chronic Inflammatory Cells

Derived from circulating blood ***monocytes***

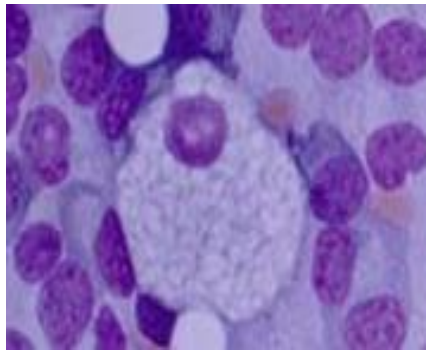
Role

- **phagocytose**
- **stimulate lymphocytes**
- **Produce cytokines**

1.Macrophages dominant in chronic infl.)

Activated macrophages

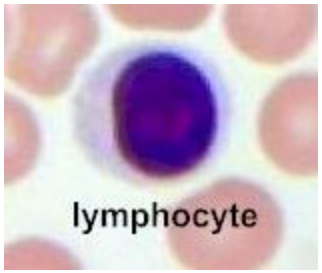
- have increased phagocytic & microbicidal activity
- called ***epithelioid cells.***
- Fuse > **giant cells**



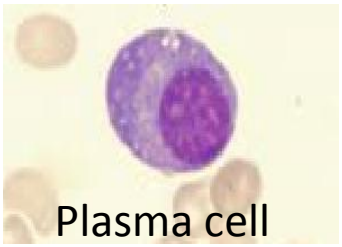
After stimulus

die or go to lymphatics.

2.lymphocytes



3.Plasma cells



4.Eosinophlis

Characteristically found in

- parasitic infections
- allergies.

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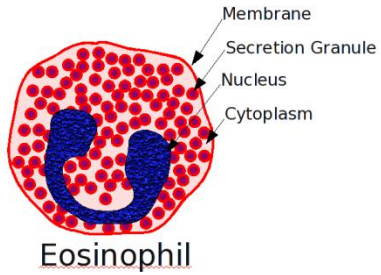


N.B.

Although neutrophils are the ***classic hallmarks of acute inflammation****, many forms of chronic infla. may continue to* **show extensive neutrophilic infiltrate**

Types of chronic inflammation

1. **Non specific**
2. **specific**

1-Chronic non specific inflammation

- ❑ They show the characteristic microscopic features of chronic inflammation
- ❑ They usually follow acute inflammation

2-Chronic specific (granulomatous) inflammation:

- ❑ Granulomatous inflammation shares the common mic features of ch. Infl
- ❑ Aggregates of activated macrophages ⟶ granuloma
- ❑ Each granuloma has a specific microscopic features distinguishing from other types
- ❑ Usually start as chronic

.

Systemic effects of chronic inflammation

- **Fever**
- **Leucocytosis** with relative lymphocytosis.
- **Cachexia**
- **↑ESR**

Differences between acute and chronic inflammation

	Acute inflammation	Chronic inflammation
Onset	Sudden	Gradual
Duration	Short	Long
Vascular phenomenon	Prominent	Less prominent
Inflammatory reaction	More exudative	More proliferative
Local (cardinal) signs of Inflammation	Prominent	Slight
Toxaemia	Acute	Chronic
Microscopy: Predominant cells	**Neutrophils** & Macrophages	**Lymphocytes, plasma cells, macrophages** & giant cells
Blood vessels	Thin-walled , dilated	Thick walled with narrow lumen
Fibrosis	Not present	Present
Changes in parenchyamatous organs	**Cloudy swelling**	**amyloidosis**
Fate	**Resolution** **Fibrosis** **Progression**	**Fibrosis**

Bacterial infection of blood

1-Toxemia:

Presence of bacterial <u>toxins</u> in blood.


Toxins

Types of toxemia:

A-Acute toxemia:

as in typhoid fever, diphtheria, pneumonia..etc.

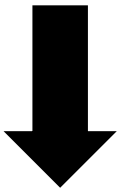
B-Chronic toxaemia as in TB

Effects and complications:

- Loss of weight.
- Normocytic anemia due to bone marrow depression.

2-Bacteremia

Presence of **small number** of bacteria in the blood which **do not multiply significantly**



- **They are commonly not detected by direct microscopy.**
- **Blood culture is done for their detection**
- **e.g. infection with Salmonella typhi, Streptococcus viridians and Escherichia coli.**

3-Septicemia

Presence of **rabidly multiplying** highly pathogenic bacteria in blood

Causative organisms:

- Pyogenic cocci
- Bacilli of plague… etc.

N.B

- It is a very serious condition with **severe toxemia and shock**.

Pathological features

4-Pyemia

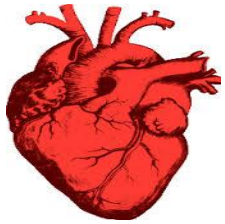
Dissemination of ***small septic emboli*** in the blood which cause their effects at the sites where they are lodged resulting in **pyemic abscesses**

Characters of pyemic abscess;

- ❑ Multiple small abscesses
- ❑ Same size
- ❑ Surrounded by **zone of congestion**
- ❑ yellowish

Pyemia

Systemic



Portal

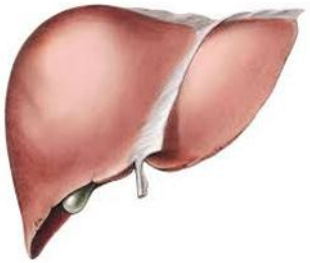
eg.GIT

venous side

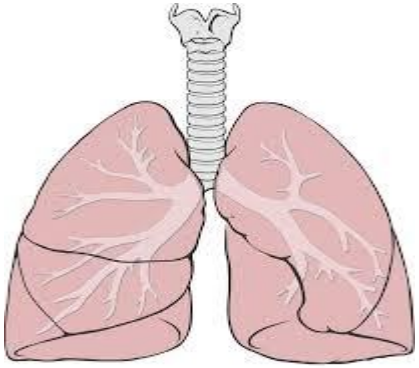
arterial side

eg.heart

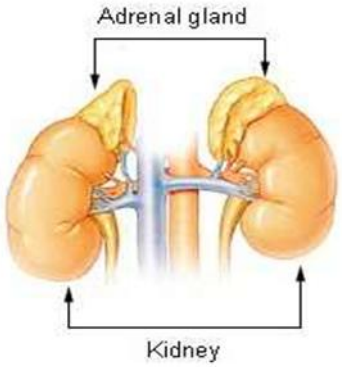
To liver



To lung



To brain, liver, kidney, spleen



Types of pyemia

Systemic pyemia	*Portal pyemia*
Septic emboli are carried by <u>systemic circulation</u>	**Septic emboli are carried by <u>portal circulation</u>**
As in : a) Acute hematogenous osteomyelitis b) Puerpural sepsis c) Suppurative otitis media d) Suppurative lung disease eg., abscess (emboli arising from lung veins) e) Acute bacterial endocarditis	As in : ❑Acute supprative appendicitis ❑Infected piles ❑Suppuration of gall bladder and large intestine
N.B : Emboli arising from venous side (a, b &c) produce pyemic abscesses in the lung while emboli passing in the general arterial circulation (d & e) produce pyemic abscesses in the brain, liver , kidney , spleen , skin , intestine , …. etc	**N.B** : Emboli are arrested in **the liver ,producing multiple abscesses**

A five year old child had erythematous skin of the fingers with small blisters after he has touched a pot of boiling water over the stove.
What is the type of inflammation?

A 36-year-old male has experienced mid-epigastric abdominal pain for the past 3 months. Upper endoscopy reveals a 2-cm ulceration of the gastric antrum. A biopsy of the ulcer shows angiogenesis with fibrosis and mononuclear cell infiltrates with lymphocytes, macrophages, and plasma cells. The best term for this pathologic process is

a. Acute inflammation
b. Serous inflammation
c. Granulomatous inflammation
d. Fibrinous inflammatiom
e. Chronic inflammation

A blood sample was taken from a patient which did not show bacteria but on performing a blood culture bacteria were detected . This is

a.Pyemia

b.Septicemia

c.Toxemia

d.bacteremia